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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/917,378 | 07/28/2001 | Shi-You Ding | NREL 01-35 | 9985 |

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PAUL J WHITE, SENIOR COUNSEL
NATIONAL RENEWABLE ENERGY LABORATORY (NREL)
1617 COLE BOULEVARD
GOLDEN, CO 80401-3393

| EXAMINER | |
|---|---|
| RAO, MANJUNATH N | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1652 | |

DATE MAILED: 02/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/917,378 | DING ET AL. | |
| | Examiner | Art Unit | |
| | Manjunath N. Rao, Ph.D. | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *10,11,26-34,43,44 and 63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *10 and 11* is/are allowed.

6)☒ Claim(s) *26-34,43,44 and 63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Withdrawal of the finality of the last Office action*

The finality of the last Office action is withdrawn. This is because, it has come to the attention of the Examiner that claims previously indicated as allowable cannot be allowed due to the availability of a prior art document and also due to non-enablement issues. A new non-final rejection follows hereby. Any inconvenience caused to the applicant is regretted.

Applicants' amendments and arguments filed on 10-31-03, have been fully considered and entered.

Claims 10-11, 26-34, 43-44, and 63 are currently pending and are present for examination.

### *Claim Objections*

Claims 10-11 are objected to because of the following informalities: Claims 10-11 recite the phrase "mannanase A peptide" which leads one skilled in the art to that it comprises less number of amino acids than in a polypeptide. However, said enzyme appears to be a polypeptide. Examiner urges applicants to amend the claim to recite "polypeptide" in order to maintain reasonable accuracy and uniformity in claim language. Appropriate correction is required.

Claims 10-11 are objected to because of the following informalities: Claims 10-11 recite the phrase "purified mannanase A". A perusal of the specification indicates that ManA is a

mannanase. However, the specification does not make any reference to a "mannanase A". Examiner urges applicants to amend the claim to recite "purified ManA mannanase" or the like in order to maintain reasonable accuracy and uniformity in the claim language.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-34, 43-44 and 63 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mannanase with ß 1,4-mannosidase activity having the amino acid sequence SEQ ID NO:1 or comprising a sequence of SEQ ID NO:3:4:5 in that order and a fusion protein comprising the above amino acid sequences, does not reasonably provide enablement for any such enzyme or fusion proteins comprising such enzyme wherein said enzyme comprises an amino acid sequence that has at least 70% or 90% sequence identity to amino acid sequence SEQ ID NO:1 or comprising a sequence of SEQ ID NO:3:4:5 in that order. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the

prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 26-34, 43-44 and 63 are so broad as to encompass any mannanase comprising an amino acid sequence having 70% or 90% identity to SEQ ID NO:1 or a polypeptide comprising a sequence of SEQ ID NO:3:4:5 in that order. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of mannanases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a single mannanase comprising SEQ ID NO:1 or comprising a sequence of SEQ ID NO:3:4:5 in that order. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching the use of SEQ ID NO:1 or polypeptide comprising a sequence of SEQ ID NO:3:4:5 in that order as a mannanase but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the

claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any mannanase with 70% or 90% identity to the enzymes comprising SEQ ID NO:1 or comprising a sequence of SEQ ID NO:3:4:5 in that order because the specification does not establish: (A) regions of the protein structure which may be modified without affecting mannanase activity; (B) the general tolerance of mannanases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue in any mannanase polypeptide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including mannanases with an enormous number of amino acid modifications to SEQ ID NO:1 or polypeptide comprising a sequence of SEQ ID NO:3:4:5 in

that order. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of mannanases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 26-27, 44 and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al. (World J. Microbiol. Biotechnol., 1990, Vol. 6(3):245-254). This rejection is based upon the public availability of a printed publication. Claims 26-27, 44 and 63 of the instant application are mannanase enzyme comprising an amino acid sequence that is at least 70% or 90% identical to SEQ ID NO:1 or SEQ ID NO:3:4:5 in that order and composition comprising the same and a method of reducing hemicellulose in a starting using said polypeptides. Johnson et al. disclose the isolation and purification of such a mannanase A, a composition comprising the same and a similar method of using said polypeptides. Johnson et al. do not disclose the amino acid sequence of said polypeptides. However, as applicants have claimed variants of SEQ ID NO:1 or SEQ ID NO:3:4:5 in that order (i.e., polypeptides that are either 70% or 90% identical to said SEQ Ids), Examiner takes the position that the enzyme of the

reference inherently has an amino acid sequence that could be either 70% or 90% identical to that of SEQ ID NO:1 or SEQ ID NO:3:4:5 in that order. Therefore Johnson et al. anticipate above claims as written based on inherency.

Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28-34, 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al. as applied to claims 26-27, 44 and 63 above, and further in view of the reasonable common knowledge regarding determining the amino acid sequence of a polypeptide and making of fusion proteins with a peptide tag such as 6-His or substrate targeting moieties, oligomerization inducers etc. Claims 28-34 and 43 are drawn to a fusion protein comprising mannanase polypeptides that are either 70% or 90% identical to SEQ ID NO:1 or SEQ ID NO:3:4:5 in that order.

The reference of Johnson et al. as it applies to claims 26-27, 43 and 64 has already been discussed above.

The art is rich in methods of making a variety of fusion proteins using heterologous polypeptides for substrate targeting (such as binding domains), 6-His for affinity purification etc. Several commercial kits are available in the art along with custom methods for individual applications.

Therefore, with the reference of Johnson et al. which provides a purified mannanase, it would have been obvious to those skilled in the art to determine the amino acid sequence of the mannanase of the reference and construct a variety of fusion proteins such as those claimed in the above claims. One of ordinary skill in the art would have been motivated to do so in order to make large quantities of the Johnson et al. enzyme and exploit the commercial value of such enzyme. One of ordinary skill in the art would have a reasonable expectation of success since Johnson et al. provide the purified enzyme and the art provides techniques for making and using a variety of fusion proteins.

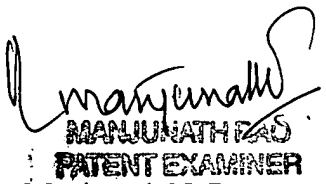
Therefore, the above invention would have been *prima facie* obvious to those skilled in the art.

***Conclusion***

Claims 10 and 11 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The examiner can normally be reached on 6.30 a.m. to 3.00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0939. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.




Manjunath N. Rao
February 3, 2004